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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,375	09/24/2001	Ikunoshin Kato	KATO18	8012

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,375	KATO ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/17/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 9/3/04. The amendment has been entered. Claims 8, 42 and 43 are currently pending in the application and are examined herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/17/04 is acknowledged. The information disclosure statement is being considered by the examiner (see attached form 892). It is noted that, with respect to references AQ, AR, and AS, the Office only received abstracts and not complete references. The cited references are being considered only t the extent of the submitted material. That is, only the abstracts of references AQ, AR and AS are being considered by the Examiner. Should applicants wish to have each reference considered in its entirety, applicants should submit the cited references in full (i.e., the entire reference should be submitted, not just the abstract).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a composition for gene therapy comprising active ingredients. With respect to the active ingredients, claim 8 recites the phrases "an effective amount of a retrovirus" (see line 4), "an effective amount of a functional substance" (see lines 7-8), and "an effective amount of vascular endothelial cells" (see lines 11-12); however, there is no indication in the claims what constitutes "an effective amount" of any of the active ingredients, nor is there an indication of what the amount is effective for. Therefore, the claims are indefinite because the metes and bounds of "an effective amount" cannot be determined and it is not clear what the effective amount is for (an amount effective for what?). Claims 42 and 43 are rejected because they are dependent claims.

Claim 42 recites the limitation "the target cell" in line 5. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a composition for gene therapy used for treating a disease susceptible to gene therapy, which contains as active ingredients an effective amount of a functional substance having heparin-II-binding domain of fibronectin (emphasis added). Therefore, the claims encompass a composition that comprises a genus of "functional substances" wherein the genus comprises a vast number of different species.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164).

In the instant case, the claims encompass a genus of "functional substance(s) having heparin-II-binding domain of fibronectin". Looking to the specification for guidance, the specification does not explicitly define explicitly define a "functional substance having heparin-II-binding domain of fibronectin". Furthermore, the only substances having a heparin-II binding domain of fibronectin found in the specification is fibronectin itself and specific domain within fibronectin (i.e., heparin-II binding domain), as well as retronectin. Given the broadest reasonable interpretation, the phrase "functional substance having a heparin-II binding domain of

fibronectin" encompasses any functional substance wherein the functional substance has a heparin-II binding domain of fibronectin. Therefore, the genus encompass different molecules including fibronectin itself, as well as fusion proteins, antibodies or virus engineered to comprise the heparin-II binding domain of fibronectin. However, the functional substances encompassed by the claims include substance which are not structurally or functionally related. Therefore, there is no structure common to all members of the claimed genus, nor is any structure/function relationship apparent. As such, the specification has not adequately described a representative number of species molecules of the genus encompassed by the claims.

It is noted amending claim 8 such that the composition encompasses a specific functional substance having a heparin-II-binding domain of fibronectin would obviate this rejection.

In view of the written description rejection above, claims 8, 42 and 43 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As mentioned in the written description rejection above, the claims encompass a genus of functional substances which the specification has not adequately described. Without a clear indication of the functional substances encompassed by the claims one of skill in the art would not know how to make and use the claimed invention without performing an undue amount of additional experimentation to first determine the functional substances encompassed by the claims.

In addition and separate from the above rejection, claims 8, 42 and 43 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

A composition for transfecting a lymphocytic leukemia cell in vitro wherein the composition comprises:

(1) a retroviral vector that operably encodes and expresses a gene of interest;

(2) a heparin-II binding domain of fibronectin; and

(3) a human umbilical cord vein endothelial cell (HUVEC)

does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a composition for gene therapy.

The breadth of the claims

As currently written, the claims are very broad and encompass a composition for treating (i.e., completely eliminating and/or preventing any future occurrence of) any disease that is susceptible to gene therapy wherein the composition can comprise 1) any one of a vast number of different functional substances that have a heparin-II binding domain of fibronectin and 2) any vascular endothelial cell.

The unpredictability of the art and the state of the prior art

As indicated above, the claims are very broad, and in general, encompass a gene therapy composition for treating any disease susceptible to gene therapy. It is respectfully pointed out that "treating" encompasses completely eliminating (i.e., curing) as well as preventing any future occurrence of the disease. Scanning the prior art, no references can be found that indicate gene therapy can be effective for either 100% curing and/or 100% preventing a disease. The prior art appears to indicate the heparin-II-binding domain of fibronectin was known as a molecule that had an affinity for retroviral vectors, and could be useful for helping the retroviral vector infect a target cell. However, there is nothing found in the prior art which indicates that the heparin-II binding domain of fibronectin can be incorporated into any functional substance and still be useful for helping a viral vector infect a target cell.

Furthermore, the claims are drawn to a composition that is claimed to be useful for treating a disease susceptible to gene therapy. As such, the claims encompass a gene therapy composition for treating any disease susceptible to gene therapy. However, there is no teaching in the prior art that all functional substances containing the heparin-II binding domain of fibronectin and all vascular endothelial cells could be used to enhance transfection of a target cell

with a retroviral vector. Considering the complex nature of biochemical interactions, it is unpredictable that any functional substance having a heparin-II binding domain of fibronectin and any vascular endothelial cell would enhance the transfection of any specific target cell.

Working Examples and Guidance in the Specification

The specification describes a working example (see example 4) wherein composition comprising a retroviral vector that expresses GFP, retronectin (which comprises a heparin-II-binding domain of fibronectin), human umbilical cord vein cells (HUVECs) and L1210 lymphocytic leukemia cells was used to transfect IN VITRO L1210 cells with the nucleic acid encoding GFP (indicated by the expression of GFP in the L1210 cells). The results indicate that the nucleic acid encoding GFP is transferred into and expressed in the target L1210 cells IN VITRO (see Example 4).

Quantity of Experimentation

Additional experimentation is required in order for one of skill in the art to be able to make and use the claimed invention to the full scope encompassed by the claims. For instance, additional experimentation would be required to determine which functional substances having a heparin-II binding domain of fibronectin, as well as which vascular endothelial cells would be functional in a gene therapy method involving delivery of a retroviral vector. Furthermore, additional experimentation would need to be performed in order to determine if vascular endothelial cells as a whole have affinity for specific target cells and if the vascular endothelial cells have affinity for any cells other than L1210 cells.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the limited knowledge of the art, the limited amount of working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

Response to Arguments

Applicant's arguments filed 9/3/04 have been fully considered but they are not persuasive.

With respect to applicants argument with respect to the rejection of claims under 35 USC 112, 2nd paragraph, the amendment was sufficient to overcome the rejection. However, the amended claims are rejected under 35 USC 112, 2nd paragraph for the reasons set forth above. The rejection is necessitated by the amendment.

With respect to applicants argument with respect to the rejection of claims under 35 USC 112, 1st paragraph, the amendment/arguments were sufficient to overcome the previous rejection. However, the amended claims are rejected under 35 USC 112, 1st paragraph (written description) for the reasons set forth above. Specifically, the claims have been amended such that they encompass a genus of functional substances wherein the functional substances have a heparin-II binding domain of fibronectin. It is noted that a functional substances have a heparin-II binding domain of fibronectin was not a limitation of the previous claims. Therefore the rejection is necessitated by amendment.

With respect to the rejection of claims under 35 USC 112, 1st paragraph for not being fully enabled, the applicants argue,

> "As regards the presently pending claims 8, 42 and 43, they are fully enabled, applicants again noting the full enabling disclosure of Examples 4 and 5, and the fact that those skilled in the present are highly skilled persons. Even if some experimentation were necessary, not conceded, such experimentation would only be routine, and that is fully permissible. The PTO has no basis for disbelieving what is set forth in applicants' specification." (see p. 7 of the response filed 9/3/04).

In response, examples 4 and 5 only enable the claims the extent indicated above. Specifically, the specification only enables the claims for a composition for transfecting a lymphocytic leukemia cell in vitro wherein the composition comprises: (1) a retroviral vector that expresses a gene of interest; (2) retronectin (or a heparin-II binding domain of fibronectin); and (3) a human umbilical cord vein endothelial cell (HUVEC)). The examples do not enable the claims for any functional substances having a heparin-II binding domain of fibronectin nor for any vascular endothelial cell, for the reasons set forth above.

With respect to the rejection of claims under 35 USC 102, the rejections are withdrawn in view of the amendment and arguments filed 9/3/04.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art unit 1635

DAVE T. NGUYEN
PRIMARY EXAMINER